collection, focused on the higher risk women but embracing the entire female population, the women with carcinoma in situ could be detected and treated, and serious illness and mortality from this important carcinoma eliminated.

ACKNOWLEDGMENT—It is a pleasure to express appreciation to the Bureau of Cancer Control, New York State Department of Health; the Connecticut State Department of Health; Dr. J. E. Dunn, Jr.; Dr. F. E. Lundin; and Dr. F. E. Bryans for permission to reproduce data from their published reports. We are also grateful to the American Journal of Public Health, the American Journal of Obstetrics and Gynecology, the Journal of the International College of Surgeons, and the Journal of the National Cancer Institute for permission to publish these data originally appearing in these journals.

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This paper was presented before the Epidemiology Section of the American Public Health Association at the Ninety-Fourth Annual Meeting in San Francisco, Calif., November 1, 1966.

## II. MARITAL AND COITAL FACTORS IN CERVICAL CANCER

Clyde E. Martin, Ph.D.

In this paper I can hardly do more than touch on the significant results presented in a recent dissertation on the epidemiology of cervical cancer which is somewhat unusual in approach, and present a portion of the logic and results of that endeavor. Three lines of investigation were followed in search of an epidemiologic explanation. Initially, the literature was reviewed for evidence

of marital and sexual phenomena which appeared to be related to a history of cervical cancer or which characterized populations known to have relatively low or high rates. Factors regarded as particularly promising in these respects were examined in detail for clues as to the temporal, causal, or statistical character of their interrelationships. A new retrospective study based upon Jewish

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Table 1—Percentages of ever-married women reporting: marriage before 20 years of age, marital dissolution, and marriage more than once

| No. of women |              | Married<br>before age 20 |       | Ever marital dissolution |            | Married more than once |            |               |
|--------------|--------------|--------------------------|-------|--------------------------|------------|------------------------|------------|---------------|
| Study        | Cases<br>No. | Controls<br>No.          | Cases | Controls                 | Cases<br>% | Controls<br>%          | Cases<br>% | Controls<br>% |
| (1)          | 288          | 553                      | 25    | 16                       | 45         | 29                     | 17         | 11            |
| (2)          | 587          | 851                      | 59    | 37                       | 56         |                        | 31         |               |
| (3)          | 523*         | 523*                     | 45    | 24                       | 21         | 7                      |            |               |
| (4)          | 194          | 207                      | 46    | 14                       | 36         | 16                     |            |               |
| (5)          | 100*         | 100*                     | 47    | 27                       | 43         | 13                     |            |               |
| (6)          | 232†         | 5,681                    | 51    | 30                       | 71         | 47                     | 51         | 26            |
| (7)          | 121          | 117                      | 71    | 49                       |            |                        | 47         | 16            |
| (8)          | 354          | 594                      | 54    | 33                       |            |                        | 30         | 14            |
| (9)          | 215          | 391                      | 68    | 53                       |            |                        | 35         | 22            |

\* Samples may include a small but unknown number of single women.

\*Samples may include a small but unknown number of single women.
†Sample of case women includes 80 with invasive carcinoma, 152 in situ carcinoma.
Authors and sample characteristics: (1) Boyd and Doll (1964), women in English hospitals; (2) Gilliam (1951), various United States hospitals, white patients (data on marital dissolution and remarriage, unpublished); (3) Lombard and Potter (1950), Massachusetts women, racially mixed; (4) Murphy (1952), Pennsylvania white women; (5) Stephenson and Grace (1954), New York City women, racially mixed; (6) Stern and Dixon (1961), Los Angeles Cancer Detection Clinic, racially mixed; (7) Terris and Oalmann (1960), Charity Hospital, New Orleans, racially mixed; (8) Wynder, et al (1954), various United States hospitals, white women; (9) Wynder, et al. (1954), various United States hospitals, Negro women.

women was then undertaken in order to explore the significance of findings emerging from the preceding analysis. Finally, an explanatory model was formulated on the basis of these studies and appears to be compatible with the many distributive features of the disease. Each area of inquiry will be discussed.

### Review of the Literature

Three factors were identified as being "primary" in that they stand in a nearperfect relationship with the occurrence of cervical cancer, namely: a nearabsence of the neoplasm among species other than the human, a near-absence of the disease among nuns, and a nearabsence of virgins among women with the diagnosis. With reference to the last observation, about one per 1,000 in Kottmeier's1 series of Swedish women were found to be virgin at diagnosis, while my compilation of data based upon studies of United States women shows about four per 1,000 as being virgin at diagnosis. These and other observations lead to the conclusion that cervical cancer is uniquely a human disease, that coital experience is prerequisite to the squamous-cell form of the disease, and that virgin females of any age are essentially at no risk of the disease.

The three marital attributes shown in Table 1 are also regularly found in association with the cancer. These attributes are: marriage before the age of 20, a history of marital dissolution, and a history of remarriage. These data appeared promising because it has long been known to social scientists that, among women, early marriage, unsatisfactory marriage, and broken marriage are correlated within the life history. Following this lead and utilizing data from studies by Wynder, et al.,2 Boyd and Doll,3 and others, it proved possible to demonstrate how the experiential events of early marriage, early coitus, early pregnancy, marital dissolution, and remarriage are all interrelated within the experience of women generally, and to further show that each of these events occurs more frequently in the lives of case women than their controls.

Figure 1 will make clearer the mutuality of association of these factors within the life history. Conceptually, this model is quite useful. It shows that if marital dissolution, for example, is a significant etiologic factor, then because disproportionate numbers of case women will be found to have had broken marriages, they will also be found to have had disproportionate experience of early marriage, early coitus, early pregnancy, and second marriage. In short, the model indicates that because all these events are interrelated within the experience of individuals, if any one event is, indeed, critical for carcinogenesis, all will appear as correlates of the disease in retrospective data.

It is not likely that any one factor in Figure 1 can be shown to be of etiologic significance by available statistical procedures. However, the knowledge that each factor is related to all other factors and is distinctive of women with cervical cancer suggests that if the relevance of any one factor to the cancer can be determined, then it becomes possible to account for the association of the entire set of factors with cancer status. Present interpretation is that age at first coitus fulfills such a criterion. As a statistic, it describes the upper limit of time each individual has spent

in the virgin state—an interval at no risk of the cancer. When coitus first occurs at an early age, the no-risk interval is minimal; when first coitus occurs at a later age, this interval is increased. Thus, age at first coitus acts as a selective factor describing that point in time when individuals leave the category at no risk, and enter the category of being at risk. Furthermore, because age at first coitus and age at marriage tend to be closely associated in time, the selective effects of age at marriage for stability of marriage also become apparent in data obtained retrospectively.

A number of observations may be cited in support of the view that the key epidemiologic factor described in Figure 1 is marital instability. Unstable marriage is known to be associated with unstable sexual relationships, and with illegitimacy, venereal infection, prostitution, and emotional problems-all of which appear in various studies as correlates of the cancer. My own examination of the literature concerning various aspects of the sexual history in relation to cancer status also indicated that with the exception of the factors, early coitus and a multiple number of sexual partners, no aspect of female sexuality appeared to be consistently or importantly associated with the disease. And while no studies of the sexuality of the males involved have been reported, present

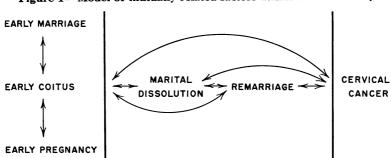


Figure 1-Model of mutually-related factors within the life history

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Table 2—Groups of women found to be at relatively low and high risk of cervical cancer

| Low risk groups   | High risk groups  |  |  |  |
|---|---|--|--|--|
| Moslem women<br>(Kmet, et al., 1963 <sup>10</sup> Wynder, et al., 1954 <sup>2</sup> )                             | Puerto Rican women (Haenszel and Hillhouse, 1959 <sup>11</sup> )  |  |  |  |
| Amish women*<br>Jewish women  | Mexican immigrant women (Haenszel, 1961; <sup>18</sup> Slate and Merritt, 1962 <sup>19</sup> )                          |  |  |  |
| (Haenszel and Hillhouse, 1959; <sup>11</sup> Kennaway, 1948 <sup>12</sup> )                                       | Negro women (Haenszel and Hillhouse, 1959 <sup>11</sup> )   |  |  |  |
| Seventh-Day Adventist women (Lemon, et al., 1964; <sup>13</sup> Wynder, et al., 1959 <sup>14</sup> )              | Inmates of a women's prison (Pereyra, 1961 <sup>20</sup> )  |  |  |  |
| Irish immigrant women<br>(Haenszel, 1961 <sup>15</sup> )  | Prostitutes<br>(Røjel, 1953 <sup>21</sup> )   |  |  |  |
| Italian immigrant women<br>(Haenszel, 1961 <sup>15</sup> )  | Venereal disease clinic patients (Greene, et al., 1965 <sup>22</sup> )  |  |  |  |
| Protestant and Catholic women who regularly<br>attend religious services<br>(Naguib, et al., 1966 <sup>16</sup> ) | Protestant and Catholic women who rarely or<br>never attend religious services<br>(Naguib, et al., 1966 <sup>18</sup> ) |  |  |  |
| Women of high economic status<br>(Dorn and Cutler, 1959 <sup>17</sup> )   | Women of low economic status<br>(Dorn and Cutler, 1959 <sup>17</sup> )  |  |  |  |
| Rural women<br>(Levin, et al., 1960 <sup>18</sup> )   | Urban women (Levin, et al., 1960 <sup>18</sup> )  |  |  |  |

<sup>\*</sup>Unpublished data compiled by Mr. Kenneth Polen, Pomerene Memorial Hospital, Millersburg, Ohio; courtesy of Dr. Harold E. Cross, Johns Hopkins School of Medicine (Feb.), 1966. One in situ and one invasive carcinoma of the squamous-cell type were discovered in the course of obtaining amears from about 1,900 Amish women, as of January, 1966—a rate considerably lower than that found among non-Amish women utilizing the same hospital.

evidence clearly supports the inference that the sexual partners of case women are more likely to have had unstable marital and sexual relationships than the partners of controls.

The view that instability of marriage is importantly related to cancer occurrence is also borne out by the characteristics of groups found to have unusually low or high rates of the cancer (see Table 2). Inspection of the lists of groups in the two columns makes evident the fact that membership in certain religious groups is associated with a low risk of the disease, whereas the high risk column tends to show a predominance of groups of low socioeconomic status. These data indicate a close correspondence between the distribution of the cancer and the distribution of patterns of unstable marriage across social groups. In effect, religious and socioeconomic orientations are seen as determinants of marital stability and the stability of sexual relationships, as well as serving as important variables for epidemiologic description.

# Report of New Retrospective Data

Further investigation took the form of a new retrospective study of 40 Jewish women previously diagnosed as having invasive or in situ squamous-cell carcinoma, and as controls, 36 Jewish women with a recent hysterectomy, known to be free of uterine cancer. Limitation of the study to the Jewish group provided an indirect control of the circumcision status of coital partners classified by Jewish-Gentile status. The possibility existed as well that, by selecting

a group at low risk of the cancer, whatever etiologic factors were present would appear in greater disparity than would be the case were the study based on a high risk group or one of heterogeneous composition.

Merits of the study include the fol-

lowing: patients were privately interviewed, usually in their homes; at interview all patients were well past hospitalization and many of its disturbing connotations; the investigator conducted all interviews; the data obtained deal more fully and systematically with both

Table 3—Number of patients: eligible according to medical record,\* interviews refused and interviews completed, by medical facility

|  | No. of patients |          |                  |  |
|--|-----------------|----------|------------------|--|
| Medical facility   | Eligible        | Refused  | Inter-<br>viewed |  |
| Abraham Jacobi Hospital, Bronx<br>Cases, 1959-Aug., 1964 | 0               | _        | _                |  |
| Beth Israel Hospital, New York City<br>Cases             | 7               | 0        | 0                |  |
| Brookdale Hospital Center, Brooklyn                      |                 |          |                  |  |
| Cases  | 13              | 0        | 2                |  |
| Controls   | 9               | 1        | 4                |  |
| Hospital of the University of Pennsylvania               |                 |          |                  |  |
| Cases  | 11              | 0        | 6                |  |
| Controls   | 10              | 1        | 5                |  |
| Jewish Hospital of Brooklyn                              |                 | _        |                  |  |
| Cases  | 23              | 0        | 9                |  |
| Controls   | 5               | 0        | 5                |  |
| The Johns Hopkins Hospital, Baltimore Cases, 1960-1963   | 0               | _        |                  |  |
| Kings County Hospital, Brooklyn<br>Cases, 1959-1963      | 0               | _        | _                |  |
| Long Island Jewish Hospital, L. I.                       |                 |          |                  |  |
| Cases  | 4               | 1        | - 3              |  |
| Controls   | 6               | 3        | 3                |  |
| Maimonides Hospital, Brooklyn                            |                 |          |                  |  |
| Cases  | 5               | 0        | 2                |  |
| Controls   | 5               | 2        | 2                |  |
| Montefiore Hospital, Bronx                               |                 |          |                  |  |
| Cases  | 11              | 0        | 6                |  |
| Controls   | 7               | 2        | 5                |  |
| Mount Sinai Hospital, New York City                      | 2               |          |                  |  |
| Cases  | .6              | 1        | 4                |  |
| Controls   | 14              | 5        | 8                |  |
| Sinai Hospital of Baltimore                              |                 | •        | _                |  |
| Cases<br>Controls  | 11<br>7         | 0<br>2   | 6<br>5           |  |
|  | •               | <b>-</b> | J                |  |
| Strang Clinic, New York City<br>Cases                    | 8               | 2        | 4                |  |
| Totals   | 162             | 20       | 79               |  |

<sup>\*</sup> For criteria, see footnote, Table 4.

Table 4-Attrition of eligible patients, by type of loss

|  |       | No. of patients |       |  |
|--|-------|-----------------|-------|--|
| Patient classification   | Cases | Controls        | Total |  |
| Patients: eligible according to medical record*  | 99    | 63              | 162   |  |
| Loss: no introduction to patient's physician   | 22    | 0               | 22    |  |
| Patients: eligible by introduction to physician  | 77    | 63              | 140   |  |
| Loss: patient deceased   | 6     | 0               | 6     |  |
| Loss: physician declined introduction to patient   | 7     | 5               | 12    |  |
| Loss: introduction not feasible (patient moved)  | 4     | 0               | 4     |  |
| Patients: introduction furnished by physician  | 60    | 58              | 118   |  |
| Loss: investigator unable to contact patient Loss: interview request withdrawn (patient ill, | 4     | 2               | 6     |  |
| hospitalized, spoke no English)  | 5     | 2               | 7     |  |
| Loss: access to patient denied by husband or relative  | 5     | 1               | 6     |  |
| Loss: interview requested, patient refused   | 4     | 16              | 20    |  |
| Patients: interview completed  | 42    | 37              | 79    |  |
| Loss: patient Jewish only by marriage  | 2     | 1               | 3     |  |
| Interviews available for analysis  | 40    | 36              | . 76  |  |

<sup>\*</sup> Criteria: designated self as Hebrew at admission, born since 1899, ever-married, believed to be living and to speak English. Cases: diagnosed as squamous-cell or in situ carcinoma of the uterine cervix, and meeting the above criteria. Controls: total er partial hysterectomy in past two years, with no history of cancer, and meeting the above criteria.

the personal and social aspects of marriage and coitus than is usually the case; and data were collected in a manner which permitted most responses to be reduced to numerical or dichotomous form for simple but statistical treatment.

Areas of the life history which it appeared profitable to explore in such a study were indicated by the observed association between the disease and marital instability, the evident need for a detailed survey of properties of the coital history, a need for new information about various attributes and behaviors of husbands and other coital partners, further assessment of the factor of psychologic stress, and the desirability of comparing cases and controls with respect to a number of characteristics which distinguish Jews from non-Jews in the general population. The study as a whole was not planned as a test of any specific hypothesis of carcinogenesis; rather, the problem of identifying what phenomena might distinguish cases and controls was left to analytic procedures.

Table 3 describes the number of patients meeting all criteria of eligibility according to medical records, by medical facility of source. While the number of patients who refused interviews the number completing interviews are indicated, details concerning sampling procedures are perhaps better described by Table 4. Of the 118 patients to whom their physicians furnished an introduction, 70 per cent of cases and 64 per cent of controls completed interviews. These differences are small but a more serious disparity occurred with respect to refusal rates, in that 7 per cent of cases and 28 per cent of controls declined to be interviewed. The effect of this and other sources of bias on the results of the study cannot determined.

Tables 5 to 10 provide a sample of the kinds of information obtained. While time does not permit their separate dis-

Table 5—Social characteristics of case and control patients

| Patient classification  | $\begin{array}{c} \text{Cases} \\ \text{No.} \!=\! 40 \end{array}$ | Controls No. = 36 |
|---|--|-------------------|
| Birth and residence   |  |                   |
| Foreign born  | 32.5%  | 19.4%             |
| Ever, rural resident  | 25.0   | 22.2              |
| including summers<br>Religious attributes                               | 25.0   | 22.2              |
| Attends or belongs  |  |                   |
| to synagogue  | 67.5   | 55.6              |
| Conservative or Orthodox  | 50.0   | 44.4              |
| Usually celebrates the  | 00.0   |                   |
| Passover holidays   | 80.0   | 83.3              |
| Occupation, husband of<br>longest duration<br>Clerical or higher status | 62.5   | 83.3              |
| S   | 02.0   | 00.0              |
| Educational attainment  |  |                   |
| Completed fewer than 10 years   | 35.0   | 25.0              |
| Some college attendance   | 25.0   | 38.9              |
| some conege attendance  | 20.0   | 30.7              |
| Family background   |  |                   |
| Father, foreign born  | 85.0   | 94.4              |
| Father, Conservative  |  |                   |
| or Orthodox   | 61.5*  | <b>80.0</b> †     |
| Reared with one or  |  |                   |
| more brothers   | 80.0   | 75.0              |
| Reared with one or  |  |                   |
| more sisters  | 72.5   | 72.2              |
| Reared as only child  | 10.0   | 5.6               |
|   |  |                   |

<sup>\*</sup> No. = 39.

cussion, I wish to draw attention to the percentage columns of Table 6. These figures illustrate the fact that more case women than controls reported: early coitus, early marriage, broken marriage, and remarriage—similar to results reported for other groups as shown in Table 1. The data suggest that whatever the significance of these factors for etiology, they are also of importance for the Jewish group. This observation appears to contradict hypotheses which attribute the infrequency of this cancer among Jewish women to genetic factors, diet, traditional habits of hygiene,

or some unusual degree of resistance or immunity.

Briefly, no significant differences were found between cases and controls with respect to: Jewish ancestry, the use of tobacco or alcohol, a history of acute episodes of emotional stress, coital abstinence at the menses, prepubescent sexual experience, frequency of coitus, the duration of coitus in years, or quantity of coitus prior to diagnosis. Many of the minor differences which appeared could have been anticipated on the basis of Table 6. More cases than controls reported dating at an early age; commented that coitus was sometimes disliked; described husbands as not sexually attractive; and denied that sexual relations had ever been important in their lives.

Factors showing a marked differentiation between the two groups are shown in Table 11 prior to summary analysis. After excluding factors d, f, and h on logical grounds, the seven remaining factors were considered with regard to their presence or absence in the life history, by case and control status. These seven factors taken in all possible combinations gave 128 fourfold tables for which chi square values were computed and ordered according to size. Maximum differentiation of the groups occurred when one or more of the fol-

Table 6—Pattern of coital and marital variables, by disease status

| Patient classification                   | Cases<br>No.=40 | Controls<br>No. = 36 |
|--|-----------------|----------------------|
| First coitus before age 20               | 52.5%           | 30.6%                |
| Married before age 20                    | 42.5            | 27.8                 |
| Ever separated, widowed, or divorced     | 37.5            | 19.4                 |
| Married more than once                   | 20.0            | 11.1                 |
| Married at diagnosis                     | 82.5            | 94.4                 |
| Married once, still married at diagnosis | 62.5            | 80.6                 |

<sup>†</sup> No. = 35.

Table 7—Jewish relationships and circumcision status of husbands

| Comparison criteria                              | Cases<br>No.=40 | Controls<br>No. = 36 |
|--|-----------------|----------------------|
| Patients: fewer than four<br>Jewish grandparents | 5.0%            | 0.0%                 |
| First husband: less than two Jewish parents      | 17.5            | 0.0                  |
| Any husband: less than two Jewish parents        | 17.5            | 0.0                  |
| First coital partner:<br>non-Jewish male         | 17.5            | 0.0                  |
| Ever, coitus with a non-Jewish male              | 22.5            | 5.6                  |
| Ever, married to an<br>uncircumcised non-Jew     | 10.0–12.5*      | 0.0%                 |

<sup>\*</sup>One patient was married for three months at age 16 to a Catholic male of unknown circumcision status. The given percentages cover alternate assumptions.

Table 8—Coital frequencies

| Patient   | Ca  | ses  | Controls |      |
|---|-----|------|----------|------|
| classification  | No. | %    | No.      | %    |
| Maximum number of<br>coital events, ever in<br>any single week of<br>marriage: 7 or<br>more times | 40  | 57.5 | 36       | 63.9 |
| Coital frequency, first<br>year or two of first<br>marriage: 3 or more<br>times per week*         | 37  | 48.6 | 35       | 51.4 |
| Coital frequency, durin<br>the several years<br>preceding diagnosis:<br>1 or more times           |     |      |          |      |
| per week  | 40  | 55.0 | 36       | 58.3 |

\* Marriages of less than six months duration were excluded from the analysis.

lowing three factors were taken into account: factor a (two or more coital partners before diagnosis), factor b (a history of at least one induced abortion), and factor e (any husband, extramarital sexual relations). According to Table 12, some 75 per cent of case women as

compared to 25 per cent of controls reported the presence in their life histories of at least one of the three factors.

### Interpretation and Conclusions

That a larger proportion of women with cervical cancer than controls in our series should have had two or more sexual partners was not unexpected in the light of their greater marital instability and longer length of time spent in the postmarital state. The finding is in accord with studies by Terris and Oalmann<sup>9</sup> and by Stephenson and Grace,<sup>7</sup> where disproportionate numbers of case women reported a history of broken marriage and/or remarriage, as well as sexual contacts outside marriage. The factor is also compatible with the association of the cancer with marital disso-

Table 9—Coital partners prior to diagnosis

| Cases<br>No. == 40 | Controls<br>No. = 36                       |
|--------------------|--|
| 22.5%              | 11.1%                                      |
| 42.5               | 16.7                                       |
| 10.0               | 5.6  |
| 25.0               | 2.8  |
| 27.5               | 8.3  |
| 17.5               | 5.6  |
| 5.0                | 11.1                                       |
|                    | No.=40  22.5% 42.5  10.0  25.0  27.5  17.5 |

Note: Extramarital coitus is defined here as intercourse outside the marital relationship while living with the spouse. The evidence for the extramarital activity of the husband is of course subject to error. Only reports of near-certain knowledge were accepted as lution and remarriage as was observed in Table 1.

Twenty-five per cent of cases and 3 per cent of controls in the present study cited the fact of their husband's involvement in extramarital coitus—comparable to data from Stephenson and Grace, where 21 per cent of cases and 8 per cent of controls reported their husbands as unfaithful.

Accepting the above observations as indicative of the epidemiologic importance of unstable sexual relationships among both men and women, and as

consistent with our interpretation of the significance of religious and socioeconomic factors for stability of marriage and the stability of sexual relationships, it is proposed that squamous-cell cervical carcinoma shares many characteristics in common with communicable diseases which follow a venereal mode of transmission.

An attempt to evaluate what is, in essence, a venereal hypothesis of cervical cancer epidemiology revealed many consistencies between various of the low risk and high risk groups of Table 2 and

Table 10—Total coital years before age 35 classified by contraceptive use and technic: women 35 and older at diagnosis

|                               | Case won (No. = 3   |       | Control women (No. = 32) |       |
|-------------------------------|---------------------|-------|--------------------------|-------|
| Contraceptive use and technic | No. of coital years | %     | No. of coital years      | %     |
| No contraception              | 24.5                | 5.3   | 22.5                     | 5.8   |
| Condom                        | 212.0               | 45.6  | 238.0                    | 61.3  |
| Diaphragm                     | 71.0                | 15.3  | 55.5                     | 14.3  |
| Contraceptive douche          | 50.5                | 10.9  | 9.5                      | 2.4   |
| Withdrawal                    | 106.0               | 22.8  | 62.5                     | 16.1  |
| Other or unknown method       | 1.0                 | 0.2   | 0.5                      | 0.1   |
|                               |                     |       | <del></del>              |       |
| Totals                        | 465.0               | 100.1 | 388.5                    | 100.0 |

Note: The total number of coital years before age 35 (a coital year is defined as a year for which at least one coital act was reported) were obtained for each patient by substracting age at first coitus from 35 and, in turn, the number of whole years of coital inactivity during the interval. Entire years of inactivity were accounted for by illness or military service of the husband, alienation within marriage, and by restraint in the postmarital period.

From information secured in the interview concerning the consistency and duration of use of each type of contraceptive practice, and the proportional use of each practice for periods when multiple methods were employed, it was possible to distribute the number of coital years before age 35 among the various contraceptive methods. In the typical case of a marriage covering the years 23-35, the respondent reported the sole use of the condom for an initial three years, and both the condom and withdrawal in equal proportions for the remainder of the interval. Thus, 7.5 of the total of 12 coital years were allotted to the condom and 4.5 years to the practice of withdrawal.

One source of error stems from the lack of systematic questioning of patients about the length of time no contraceptives were used when conception was contemplated. This error is assumed to be small in that it seems unlikely that entire years of noncontraception would have gone unreported considering the detail of the inquiry and the intense concern with the problem of fertility control reported by numerous respondents.

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Table 11-Factors selected from foregoing tables for their value in differentiating cases from controls, by per cent of women reporting the factor, significance test of proportional differences, and phi coefficient of correlation

|      |                              | Per cent          | with factor         | Test of propor-  | Phi               |
|------|------------------------------|-------------------|---------------------|------------------|-------------------|
| Fac- | Descriptive title            | Cases<br>No. = 40 | Controls No. $= 36$ | tional<br>diff.* | coeffi-<br>cient† |
|      | Descriptive title            |                   |                     |                  |                   |
| а    | Two or more coital partners  | 42.5%             | 16.7%               | S.               | 0.259             |
| b    | Ever, induced abortion       | 42.5              | 16.7                | S.               | 0.259             |
| С    | First coitus before 20       | 52.5              | 30.6                | S.               | 0.201             |
| d    | Patient/husband extramarital | 27.5              | 8.3                 | S.               | 0.219             |
| е    | Any husband, extramarital    | 25.0              | 2.8                 | S.               | 0.285             |
| f    | First coitus with non-Jew    | 17.5              | 0.0                 | S.               | 0.224             |
| g    | Ever, coitus with non-Jew    | 22.5              | 5.6                 | S.               | 0.209             |
| h    | Married to uncir. non-Jew‡   | 12.5              | 0.0                 | S.               | 0.173             |
| i    | Foreign born                 | 32.5              | 19.4                | N.S.             | 0.121             |
| j    | Ever, marital dissolution    | 37.5              | 19.4                | N.S.             | 0.174             |

<sup>\*</sup> Tested for significance at 5 per cent level by:

$$p_1-p_2\pm 1.96 \sqrt{\frac{p_1(1-p_1)}{n_1} + \frac{p_2(1-p_2)}{n_2}}$$

† Computed by:  $\sqrt{\frac{X^2}{X^2 \text{ perfect}}}$  in which chi square is corrected for con-

tinuity. This formula is a modification of the phi coefficient:  $\sqrt{\frac{X^2}{N}}$ 

where N=perfect X<sup>2</sup> without the correction for continuity.

‡ All calculations are based on the assumption of noncircumcision in the case cited in the footnote to Table 7.

their relative rates of infection of one or another venereal disease. However, a more definitive or statistical appraisal of the postulated relationship appeared to be out of the question because of the many deficiencies of epidemiologic evidence on venereal infection. At the same time, knowledge about the social mechanisms which promote or retard the spread of venereal infection provided an alternate logic by which to consider the problem.

If we assume the existence of an infectious agent which is a necessary although insufficient condition for the occurrence of the cancer, and further assume the agent to be: (a) asympomatic for the carrier, (b) carried by the two sexes, (c) solely or primarily transmitted by coitus, and (d) such that many years may intervene between initial infection and its manifestation in women by malignancy, then it becomes completely possible for such an agent to be distributed among all human populations. That these assumptions are not without foundation is illustrated by various features of the mouse mammary tumor system<sup>23</sup> and by the realization that none of the venereal diseases exempt nations, races, or cultures despite the variability of their occurrence among population segments. There is no apparent reason why this could not also be characteristic of a carcinogenic agent whose presence has never been detected.

While our reasoning here is partly speculative, the fact seems to be that as we seek to account for the low risks of the cancer among individuals, our ability to do so proves the more successful when our explanation takes into account their insulation from a wider pool of infection. For example, we observe that virgin women are not at risk of venereal infection, two coitally inexperienced individuals who initiate and maintain an exclusive sexual relationship are hardly at risk of such infection, and that the risk increases for both parties to the relationship if either becomes involved outside the relationship. What that risk may be will of course depend upon the prevalence of infection among third parties and the number who may be involved. The relevance of this reasoning for any venereal disease is obvious enough and its applicability in the present context of a suspected infectious agent for carcinogenesis is made likely by the previously cited evidence of the importance of unstable coital relationships for etiology.

Turning again to Table 2, we are struck by the fact that Moslem, Amish, Jewish, Seventh-Day Adventist and other religiously oriented groups—groups at very low risk of the cancer—are not only doctrinal in matters of

marital and sexual conduct, but additionally practice religious endogamythat is, most members marry within their faith. Generalizing from these observations, it is proposed that the above groups are exceptionally free of the disease because of three mechanisms: (1) their high rates of endogamous marriage present a barrier to the introduction of a venereally infectious agent into their membership from sources outside religious boundaries; (2) their maintenance of monogamous sexual patterns restricts the propagation of infection within their membership, an infection which may be introduced when a small proportion of members marry or have sexual contacts with nonmembers; and (3) in the case of an agent dependent upon venereal transmission, the passing of each generation serves to deplete their membership of existing infection. If these processes are, in fact, the essential elements of an epidemiologic model, then it becomes possible to predict that any group which practices endogamous marriage, monogamous patterns of sexual behavior, and maintains its boundaries over generations by the promulgation of endogamous marriage will also be at low risk of an agent of

Table 12—Permutations of factors a, b, e as related to per cent of women included in each set of factors, values of  $X^2$ , percentage ratios of  $X^2$  to perfect  $X^2$ , and phi coefficients of correlation

|                        | Per cent of women in the set |                      | X2         | Ratios<br>X <sup>2</sup> (100) | Phi coeff.             |
|------------------------|------------------------------|----------------------|------------|--------------------------------|------------------------|
| Factors                | Cases<br>No. =40             | Controls<br>No. = 36 | <b>A</b> - | X <sup>2</sup> perfect         | X <sup>2</sup> perfect |
| a                      | 42.5%                        | 16.7%                | 4.83       | 6.70                           | 0.259                  |
| b                      | 42.5                         | 16.7                 | 4.83       | 6.70                           | 0.259                  |
| e                      | 25.0                         | 2.8                  | 5.87       | 8.15                           | 0.285                  |
| a and/or b             | 70.0                         | 22.2                 | 15.49      | 21.49                          | 0.464                  |
| a and/or e             | 52.5                         | 19.4                 | 7.53       | 10.46                          | 0.323                  |
| b and/or e             | 50.0                         | 19.4                 | 6.45       | 8.95                           | 0.299                  |
| a and/or b<br>and/or e | 75.0                         | 25.0                 | 17.01      | 23.61                          | 0.486                  |

Note: All chi squares are corrected for continuity.

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significance for this form of cancer and of all forms of venereal disease as well.

Whether this attempt to account for individual and group variation in cervical cancer risk in terms of relative isolation from a wide reservoir of infection, and whether the emergence of induced abortion as an etiologic factor in the present study actually reflect the existence of the kind of infectious agent which has been postulated are questions awaiting further investigation. However, the proposed hypothesis indicates the types of studies needed to assess its validity and the character of data to be expected if it is, indeed, the appropriate mechanism.

ACKNOWLEDGMENTS—The author wishes to acknowledge, with appreciation, the counsel and encouragement of Dr. Abraham M. Lilienfeld, chairman of the Department of Chronic Diseases, School of Hygiene and Public Health, and Dr. James S. Coleman, former chairman of the Department of Social Relations, who served as co-directors of his training and dissertation research at Johns Hopkins University; the extensive help of many physicians who assisted with the locating and contacting of selected patients for the purpose of obtaining interviews; and the splendid cooperation of the women who participated as subjects in the present study.

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This paper was presented before the Epidemiology Section of the American Public Health Association at the Ninety-Fourth Annual Meeting in San Francisco, Calif., November 1, 1966.

The investigation was supported by PHS Special Research Fellowship (Grant No. MH-12,424) from the National Institute of Mental Health. Completion of the dissertation manuscript was also supported, in part, by PHS Training Grant No. T1 CA 5165 from the National Cancer Institute.